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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,759	09/22/2004	Hyo Jeong Hong	DE1586	9699

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	
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09/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,759	HONG ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-24* is/are pending in the application.

4a) Of the above claim(s) *11-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,6,7,9 and 10* is/are rejected.

7)☒ Claim(s) *4, 5 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed June 18, 2008 in response to the Office Action of March 18, 2008 is acknowledged and has been entered. Claim 3 has been amended. Claims 2-10 are under examination. Claims 11-24 are withdrawn.

Claim Rejections - 35 USC § 112

Rejection of claims 3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendment.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 6, 7, 9 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is maintained**.

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that since the art discloses the DP7, JH4, DPK12 and JK (the human immunoglobulin germline gene segment), the skilled artisan could easily make the heavy chain DP-JH4 and the light chain DPK-JK4, and it is therefore unnecessary for Applicant to include in the specification what is already known in the prior art to satisfy the enablement requirement. Applicant cites references disclosing the DP7, JH4, DPK12 and JK. Applicant states that Figures 2a-c and 2b disclose the sequences.

In response to Applicants arguments, the Office notes that Applicant failed to state whether Applicant refers to Figures in the present Application or in the cited references.

Applicant failed to state which sequences are disclosed in the figures. It is however presumed that Applicant refers to the figures in the present Application. Examiner reviewed Figures 2a-c and 2b of the present Application but did not find sequences encoding DP7-JH4 or DPH12-JK4. Figures 2a-c and 2b disclose the sequences of KR127 heavy and light chains. It is noted that KR127 is a murine antibody and DP7-JH4 or DPH12-JK4 are human antibodies heavy and light chain, respectively. As acknowledged in the Office action of March 18, 2008, the specification and the sequence listing provides SEQ ID NOs for the heavy and light chain of the KR127 antibody, however neither the specification nor the sequence listing provide the sequences of DP7-JH4 and DPH12-JK4.

In Remarks of June 18, 2008 Applicant points to Figures 2a-c and 2b however Applicant does not refer to any specific SEQ ID NOs encoding the DP7-JH4 or DPH12-JK4. The present sequence listing does not list SEQ ID NOs of the DP7-JH4 or DPH12-JK4, or the SEQ ID NO: of the KR127 that is grafted onto DP7-JH4 or DPH12-JK4. The disclosure of DP7, JH4, DPK12 and JK in the prior art is not sufficient to enable the skilled artisan to make and use the claimed antibodies, because it is unknown whether those human germline sequences have been made publicly available at the time of the invention. Only because the prior art references were publicly available at the time of the invention (as indicated by Applicant) that does not ensure the availability of the antibodies disclosed in the cited references. It is also noted that Applicant provides argument only with regard to the heavy chain DP7-JH4 recited in the claims, however Applicant dos not mention the light chain DPH12-JK4. It is noted that DPH12-JK4 and DPK-JK4 are not the same constructs. The specification discloses both DPH12-JK4 and DPK-JK4 (see page 5). It is understood that DPH12-JK4 and DPK-JK4 are two different light chains. However

the DPH12-JK4 is recited in the present claims and there is no sequence, a vector or a hybridoma cell line producing the DPH12-JK4, and Applicant did not provide arguments with regard to the availability of DPH12-JK4. Thus because it would have been undue experimentation to practice the present invention without access to DP7-JH4 and DPH12-JK4, and because Applicant did not provide sequences, vectors or a hybridoma cell lines producing the claimed constructs, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claim 2 under 35 U.S.C. 102(b) as being anticipated by Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that in contrast to the present invention where the alanine scanning mutagenesis is used in the process for humanizing the antibody for the determination of the specificity of SDR among the CDR, Leong teaches using alanine scanning mutagenesis for affinity maturation of the already humanized antibody.

In response to Applicants arguments, the Office points out that Leong discloses that his method step of alanine scanning mutagenesis is one of the method steps of making the humanized antibody (see Construction of humanized versions of anti-IL-8 antibody on page

107). It is also noted that both, prior art and Applicant's method perform alanine scanning mutagenesis for the purpose of optimizing the affinity of the murine CDR to the human antigen. The present method steps are: a) performing alanine scanning mutagenesis to optimize the affinity of the murine antibody and b) grafting the murine CDRs onto the human antibody. Leong's method steps of making the humanized antibody are: b) grafting the murine CDRs onto the human antibody and a) performing alanine scanning mutagenesis to optimize the affinity of the murine antibody to the human antigen. Thus the prior art method steps are identical with the claimed method steps and both methods arrive at the humanized antibody. Leong performs alanine scanning mutagenesis after grafting the murine antibody CDRs onto the human antibody, while in the present method the alanine scanning mutagenesis is performed first and then the murine antibody CDRs (already affinity matured) are grafted onto the human antibody. The present method does not require that step a) must necessarily precede step b). Because the method steps of the prior art are identical with the claimed method steps it is the Office position that Leong anticipates the present claim and thus the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of claim 3 under 35 U.S.C. 103(a) as being obvious over Maeng et al. (Virology, 2000 Vol. 270, p. 9-16) in view of Leong et al. (Cytokine, November 2001, Vol. 16, p. 106-119) **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that the fact that the murine monoclonal antibody KR127 is taught by Maeng and that the heavy chain of SEQ ID NO: 2 and the light chain of SEQ ID NO: 4 may inherently be present as sequences of KR127 is not an inherent teaching of the claimed process. Applicant argues that it would not be obvious to one skilled in the art to replace each amino acid residue in the CDR region of the murine monoclonal antibody and to graft the murine alanine replaced CDRs onto a human antibody.

In response to Applicant's argument, the Examiner notes that in the rejection of record Examiner did not say that Maeng inherently teaches the claimed process. Examiner said that it is the Office position that the Maeng's KR127 antibody has the same structure as the murine monoclonal antibody comprising the heavy and light chain of SEQ ID NO: 2 and SEQ ID NO: 4 of the present invention.

As disused above, the process of making humanized antibodies according to the present claims has been known at the time of the invention, as taught by Leong. The murine KR127 monoclonal antibody has been known in the prior art, as taught by Maeng. Thus it would have been obvious to humanize KR127 antibody according to the method disclosed in Leong because the KR127 antibody has binding affinity for HBV pre-S1 antigen and humanizing murine KR127 antibody could have an application for human use.

Thus because the present claims would have been obvious to the skilled artisan at the time of the invention as discussed above and on the record, the rejection is maintained.

Claim Objection

Claims 4, 5, and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-

8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648